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Symptomatic and functional remission and its associations with quality of life in patients with psychotic disorder in Assertive Community Treatment teams

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Abstract

Objectives: The aims of the present study were (1) to determine the proportion and characteristics of patients treated in Assertive Community Treatment teams who achieve symptomatic remission (SR) and/or functional remission (FR) and (2) to explore the association between both types of remission and (3) their bearing on quality of life (QoL).

Methods: Data comprised assessments from 278 patients who were repeatedly assessed using the Positive and Negative Syndrome Scale to assess SR, the Health of the Nation Outcome Scales to assess FR, and a shortened version of the Manchester Short Assessment to assess QoL. χ^2 Tests and a logistic regression analysis were used to analyze the relation between patient and treatment characteristics and achieving SR or FR. A Kruskal-Wallis test, Mann-Whitney *U* tests, and a logistic regression analysis were used to analyze the relationship between remission status and QoL.

Results: After a mean treatment duration of 2.4 years, 26% met the criteria for SR and 30% for FR. Prescription of antipsychotic medication was associated with achieving both SR and FR. Approximately half of the patients who achieved SR also achieved FR. Achieving FR was associated with better QoL. Patients in SR did not have better QoL than did patients not in SR.

Conclusions: Remission of symptoms in patients treated in Assertive Community Treatment teams was not a prerequisite for FR or vice versa. FR, not SR, was associated with better QoL.

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1. Introduction

Outcome in schizophrenia is a multidimensional construct, including symptom level, functioning, and quality of life (QoL) [1–4]. Symptomatic remission (SR) is often used to measure the success of treatment and can be defined as a state characterized by a fall in the severity of symptoms with a low to mild symptom threshold over a meaningful period [5–7]. Andreasen et al [5] proposed criteria for SR as a low to mild symptom level (positive, negative, and disorganized symptoms) for more than 6 months, with no impact on the

individual's behavior. Outcome can also be assessed in terms of functional remission (FR) [8], although, to date, no generally accepted definition of FR exists [6,9–11]. Defining FR may be more difficult because there is no societal norm or clear reference for the level of functioning in daily life (eg, about being employed, social role, independent living, and the quality of social contacts) [6,12]. Some authors propose that FR in patients with psychotic disorder consists of adequate functioning in a variety of important life domains including social relationships, productive activities, activities of daily living, and living conditions [6]. Wunderink et al [8] suggest that FR should reflect appropriate social role functioning in the main domains of everyday life, such as occupation, social relationships, citizenship, and partnership. Based on similarities in the descriptions of FR, we propose to define FR as

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adequate or no more than minimal or mild disabilities in social functioning, daily life activities, and living conditions.

To date, it is unknown whether SR is a prerequisite for FR and which one of the 2 is associated with QoL. Two recent studies [8,13] showed that patients meeting the SR criterion did have better levels of functioning than did patients not in remission. However, there was no evidence that achieving SR was an essential precondition for appropriate functioning.

Results of studies on the associations between SR and/or FR and QoL are inconsistent [6,8,14–17]. Some authors suggest that there is no clear relation between the level of functioning or symptoms and QoL [6,8], whereas others have argued that the severity of the symptoms and the level of social functioning are of importance for QoL [14–17].

Therefore, in this study, we determined the proportion of patients treated in ACT teams who achieved SR and/or FR, examined which patient and treatment characteristics were associated with achieving SR and/or FR, and explored the association between both types of remission and their bearing on QoL.

2. Methods

2.1. Setting and patients

The study involved patients with psychotic disorder from 7 ACT teams in the city of Rotterdam, the Netherlands. Criteria for treatment by an ACT team were (1) age 18 years or greater; (2) having a severe mental illness, usually a psychotic disorder, with or without a comorbid substance use disorder (SUD); and (3) a lack of motivation for regular treatment at the start of ACT that made assertive outreach necessary.

2.2. Data collection

Data from this study were obtained as part of a routine outcome-monitoring (ROM) procedure. The ROM assessments included several instruments and were planned every 6 months. The assessments were completed by independent raters (mostly psychologists) and were used in clinical practice to discuss treatment progress with the patient. Routine outcome-monitoring data collection was approved by the Dutch Committee for the Protection of Personal Data. Data for the present study were used anonymously. In addition to the ROM assessments, the following data were collected: sex, age, ethnicity (country of birth), education level, age of first contact with mental health services, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* diagnoses (as made by the psychiatrist of the ACT team), being prescribed antipsychotic medication (yes or no), and duration of treatment in ACT.

2.3. Instruments

2.3.1. Assessment of SR

To assess SR, we used 8 items of the Positive and Negative Syndrome Scale (PANSS) proposed by the

Remission in Schizophrenia Working Group [5]. *Symptomatic remission* was defined as scores of 3 or lower during a 6-month period or more for 8 items: P1 (delusions), P2 (conceptual disorganization), P3 (hallucinatory behavior), N1 (blunted affect), N4 (social withdrawal), N6 (lack of spontaneity), G5 (mannerisms/posturing), and G9 (unusual thought content).

2.3.2. Assessment of FR

We have proposed to define FR as no more than mild disabilities in social functioning, daily life activities, and living conditions. It should be emphasized that there is no generally accepted definition of FR and, thus, no specific instrument to assess it. In the present study, we used 3 items of the Health of the Nation Outcome Scales (HoNOS) to assess FR [18,19]. The HoNOS was originally developed as a standardized assessment tool for routine use by mental health services. It consists of 12 clinician-rated scales, each using 5 points from 0 (no problem) to 4 (severe/very severe). The psychometric properties of the English and Dutch HoNOS scores have been found to be acceptable [18,19]. The following 3 items were used to assess FR: (1) everyday social functioning (item 9: relationship problems); (2) activities of daily living and complex skills (item 10: problems of daily living), such as budgeting, organizing life, occupation recreation, mobility, the use of transport, and shopping; and (3) housing (item 11: problems with living conditions). Patients achieved FR if their disabilities in social functioning, daily life activities, and living conditions were no more than minimal to mild—in other words, if these HoNOS items were scored 2 or lower during a period of 6 months or more.

2.3.3. Assessment of QoL

The QoL scale of the cumulative needs for care monitor was used to measure subjective QoL [20]. This instrument was based on the Manchester Short Assessment (MANSA) of QoL scale [21]. The scale consists of 6 items [22] including financial situation, accommodation, relationship with others, physical health, psychological health, and life as a whole, which were rated on a 7-point scale (1 [“Couldn’t be worse”] to 7 [“Couldn’t be better”]).

2.3.4. Analyses

SPSS version 15.0 was used for all analyses (SPSS, Chicago, Illinois). First, we determined the proportion of patients who had been in SR and FR over the last 2 assessments. Using Pearson χ^2 test, we compared patient characteristics: sex, age (18–30, 30–40, 40–50, >50 years), ethnicity (born in the Netherlands or elsewhere), education level (none, elementary, lower high school and over), comorbid SUD (yes or no), and treatment characteristics: prescription of antipsychotic medication (yes or no) and treatment duration (0–1, 1–2, 2–3, >3 years of ACT before their assessment) between patients achieving SR and/or FR vs those who did not. We also used Pearson χ^2 test to explore the relationship between patients achieving SR and FR.

After these analyses, logistic regression analyses were performed, including baseline values and all patient and treatment characteristics as predictors of SR and FR. Note that PANSS baseline values were not included because they were not available. Logistic regression was carried out starting with a stepwise forward selection, predictors required a probability value of $P < .25$ for entry into the model, and then subsequently, the predictors were removed at a probability value of $P > .05$ using the stepwise backward elimination procedure and a log likelihood test. Next interaction terms were calculated, followed by a forward stepwise ($P > .25$) and backward elimination ($P > .05$) procedure of these interaction terms [23].

To explore the relationship between remission (SR and FR) and their bearing on QoL, we analyzed the relationship between remission status and QoL (total score) during the last ROM assessment using a Kruskal-Wallis test and Mann-Whitney U tests. Afterward, a logistic regression analysis was performed, including baseline QoL scores and remission status (SR and FR) as predictors of QoL (dichotomized via median split).

3. Results

3.1. Patients

Within all 7 ACT teams, a total of 519 patients were diagnosed as having a psychotic disorder. Routine outcome-monitoring outcome data (2 repeated complete HoNOS and PANSS assessments) were obtained from 278 patients, representing 54% of all ACT patients with a psychotic disorder. Based on the patient characteristics, these patients appeared to be representative for all ACT patients with a psychotic disorder, as we observed that the only statistical significant difference between these patient groups was that there were more male patients in our patient selection (82% in the ROM group and 77% in the total group). We observed no other statistically significant differences with respect to age, ethnicity, or education level.

Most patients were male (82.4%) and had a mean (SD) age of 41.4 (10.8) years. Only 44.2% were born in the Netherlands. Diagnosis for all patients included in the study was schizophrenia or other psychotic disorder. Forty-nine percent were also diagnosed as having a comorbid SUD. The mean (SD) treatment duration from the start of ACT was 2.4 (1.5) years, and the first contact with mental health services started about a decade before entering in ACT (mean \pm SD, 10.4 \pm 9.0 years). The period between the 2 last consecutive ROM assessments, which constituted the remission assessment period, consisted of an average (SD) timeframe of 9.6 (4) months.

3.2. Proportions of symptomatic and FR (Table 1)

Symptomatic remission was achieved by 72 (26%) of the 278 patients, and 84 patients (30%) met the criteria for FR;

160 patients (58%) achieved neither SR nor FR, and 38 patients (14%) achieved both SR and FR.

Of the 72 patients in SR, 38 (53%) also met the criteria for FR; of the 84 patients in FR, 38 (45%) were also in SR (Table 1). These data do not suggest a sequential relationship between SR and FR, indicating that SR and FR do not seem to be prerequisites for one another in this sample. The χ^2 test for the association between SR and FR ($\chi^2 = 23.457$, $df = 1$, $P < .001$), however, showed that the proportion of patients in SR who achieved FR (53%) differed from the proportion of patients who did not achieve SR but achieved FR (22%) (odds ratio, 3.887; 95% confidence interval [CI], 2.205–6.854).

Table 2 presents patient characteristics and their associations with SR and FR, respectively. These analyses showed that the presence of an SUD and the prescription of antipsychotics were associated with achieving SR. The prescription of antipsychotics was also associated with achieving FR. Logistic regression analyses (Table 3) showed that only the prescription of antipsychotics remained as an independent predictor of achieving both SR and FR.

3.3. Remission and QoL

Patients who were in SR (irrespective of FR) had higher QoL scores than did patients who were not in SR ($z = -2.338$, $P = .019$). The same was found concerning patients in FR (irrespective of SR), also reporting a significantly higher QoL compared with those who were not in FR ($z = -4.376$, $P < .001$). When patients were divided into 4 groups—(1) SR plus FR, (2) SR but no FR, (3) FR but no SR, and (4) no SR plus no FR—they showed significant differences in QoL total scores (Kruskal-Wallis test: $\chi^2 = 21.203$, $df = 3$, $P < .001$). Further analyses showed that patients who were both in FR and in SR (group 1) had better QoL scores compared with patients who were in neither FR nor SR (group 4) ($z = -4.107$, $P < .001$). However, there was no difference in QoL between patients who were only in SR (group 2) and those who were neither in SR nor FR (group 4) ($z = -0.552$, $P = .581$). Interestingly, patients only in FR (group 3) had better QoL than did patients who were neither in FR nor SR (group 4) ($z = -2.825$, $P = .005$). A logistic regression analysis confirmed these findings indicating that only FR was independently associated with QoL ($\beta = 2.584$; $P = .011$; 95% CI, 1.248–5.349) (Table 4).

Table 1

Symptomatic and FR in 278 patients after a mean (SD) of 2.4 (1.5) years of treatment in ACT teams

		FR, n (%)	NFR, n (%)	Total, n (%)
SR	n (%)	38 (R 52.8%, C 45.2%)	34 (R 47.2%, C 17.5%)	72 (R 100%, C 25.9%)
NSR	n (%)	46 (R 22.3%, C 54.8%)	160 (R 77.7%, C 82.5%)	206 (R 100%, C 74.1%)
Total	n (%)	84 (R 30.2%, C 100%)	194 (R 69.8%, C 100%)	278 (R 100%, C 100%)

NSR, no SR; NFR, no FR; n, number of patients; R, row percentage; C, column percentage.

Table 2

Characteristics of patients achieving symptomatic and FR

	N = 278 (%) ^a	n (%) ^b , in SR	n (%) ^b , not in SR	χ^2 SR	n (%) ^b , in FR	n (%) ^b , not in FR	χ^2 FR
Sex							
Male	229 (82.4)	59 (25.8)	170 (74.2)	NS	69 (30.1)	160 (69.9)	NS
Female	49 (17.6)	13 (26.5)	36 (73.5)		15 (30.6)	34 (69.4)	
Age (y)							
18–30	50 (18)	18 (36)	32 (64)	$P < .1$	21 (42)	29 (58)	$P < .1$
30–40	78 (28.1)	22 (28.2)	56 (71.8)		25 (32.1)	53 (67.9)	
40–50	84 (30.2)	23 (27.4)	61 (72.6)		26 (31)	58 (69)	
>50	64 (23)	9 (14.1)	55 (85.9)		12 (18.8)	52 (81.3)	
Missing	2 (0.7)						
Ethnicity							
Native	123 (44.2)	31 (25.2)	92 (74.8)	NS	34 (27.6)	89 (72.4)	NS
Nonnative	155 (55.8)	41 (26.5)	114 (73.5)		50 (32.3)	105 (67.7)	
Level of education							
None	26 (9.4)	8 (30.8)	18 (69.2)	NS	6 (23.1)	20 (76.9)	NS
Elementary	38 (13.7)	11 (28.9)	27 (71.1)		12 (31.6)	26 (68.4)	
Lower and over	161 (57.9)	42 (26.1)	119 (73.9)		48 (29.8)	113 (70.2)	
Missing	53 (19.1)						
Substance use							
SUD	137 (49.3)	43 (31.4)	94 (68.6)	$P < .05$	44 (32.1)	93 (67.9)	NS
No SUD	141 (50.7)	29 (20.6)	112 (79.4)		40 (28.4)	101 (71.6)	
Medication use							
Prescription of AP	202 (72.7)	60 (29.7)	142 (70.3)	$P < .05$	73 (36.1)	129 (63.9)	$P < .05$
No prescription of AP	74 (26.6)	11 (14.9)	63 (85.1)		11 (14.9)	63 (85.1)	
Missing	2 (0.7)						
Treatment duration (y)							
0–1	57 (20.5)	15 (26.3)	42 (73.7)	NS	22 (38.6)	35 (61.4)	NS
1–2	70 (25.2)	18 (25.7)	52 (74.3)		20 (28.6)	50 (71.4)	
2–3	62 (22.3)	15 (24.2)	47 (75.8)		16 (25.8)	46 (74.2)	
>3	87 (31.3)	23 (26.4)	64 (73.6)		26 (29.9)	61 (70.1)	
Missing	2 (0.7)						

 χ^2 , Pearson χ^2 test; AP, antipsychotics.^a Column percentage.^b Row percentage.

4. Discussion

4.1. Remission frequencies

Our results showed that 26% of the patients achieved SR and 30% achieved FR after a mean of 2½ years of ACT. Being prescribed antipsychotic medication was associated with achieving SR and FR. Functional remission, not SR, was associated with QoL.

4.2. Symptomatic and FR

In our study, the prescription of antipsychotic medication was related to achieving both SR and FR. It may be that the use of medication increases the chance of achieving SR and FR or that those patients accepting medication have a better prognosis, independent of the medication itself. The observational design of the present study does not allow us to determine causality.

On average, SR rates in patients from our study were slightly inferior to those found by Shida et al [24] and Lambert et al [10], who found that 1 in 3 of their patients was in SR after a period of about 1 year. A study in first-episode patients reported 52% SR over a 2-year follow-up [8]. Other

studies even reported SR rates of 60% over 3 to 5-year periods [25–27] and of 66% over a 2-year period [28]. These discrepancies are likely to be related to the duration of follow-up, treatment history and patient characteristics.

Table 3

Logistic regression analyses for the association between demographic variables, SUD, and medication use and SR and FR, respectively

		95% CI for Exp(<i>B</i>)		
	<i>β</i> (SE)	Lower	Exp(<i>B</i>)	Upper
SR				
Constant	−1.745 (0.327)*	—	0.175	—
Prescription of antipsychotic medication	0.884 (0.361) [†]	1.192	2.42	4.912
FR				
Constant	−2.171 (0.356)*	—	0.114	—
Prescription of antipsychotic medication	1.069 (0.37)*	1.409	2.911	6.013
Baseline FR	1.341 (0.284)*	2.193	3.823	6.664

SR: $R^2 = 0.036$ (Nagelkerke), Hosmer and Lemeshow goodness of fit: $\chi^2 = -$, $P = -$; FR: $R^2 = 0.171$ (Nagelkerke), Hosmer and Lemeshow goodness of fit: $\chi^2 = 4.556$, $P = .102$.

* $P < .01$.[†] $P < .05$.

Table 4

QoL total scores in ACT patients with or without symptomatic or FR

QoL total score	FR, median (IQR)	NFR, median (IQR)
SR	33 (31–37)	29 (24–34)
NSR	32 (28–35)	28 (22–34)

NSR, no SR; NFR, no FR; IQR, interquartile range.

Patients in ACT often show less treatment engagement and medication adherence, possibly leading to a relatively worse outcome. Also, our patient sample was older as compared with the study using first-episode patients. With regard to the possible impact of age, several factors may negatively influence SR. First, the impact of prolonged (untreated) illness and, second, higher age may reflect a filtering of chronically difficult to engage patients in an ACT team. Most patients treated in our ACT teams were in contact with mental health services for more than a decade. Interestingly, we found approximately the same FR rates as compared with the study by Wunderink and colleagues [8], who found FR rates of 26.4% after a 2-year period in first-episode patients using the Groningen Social Disabilities Schedule (GSDS). Other studies showed different proportions of patients achieving FR. For example, one study by San and colleagues [29] using a restrictive threshold of at least 81 points on the Global Assessment of Functioning (GAF) scale reported that social functioning was adequate in only 10.2% of all patients with schizophrenia. Another study using the World Health Organization Disability Assessment Schedule showed that only 14% of patients with schizophrenia had no functional disability after 15 years of follow-up [30]. In the present study, however, we allowed for some minimal disability, so the incongruence between these studies is likely to be related to the use of different scales and definitions of FR, which may have affected the remission rates [31]. Therefore, we were not able to make valid comparisons with other studies.

We found no evidence of a temporal sequence for SR after FR because more than half of the patients who achieved SR also achieved FR and almost half the patients who achieved FR also achieved SR. If a temporal sequence would have been the case, more patients who achieved SR would also have achieved FR or vice versa. This is only partly in line with the assumptions of Weiden and Zygmunt [32] and Priebe [4], who suggested that the presence of more symptoms is associated with worse functioning. Based on our data, however, it does not seem necessary to focus on achieving SR first to achieve FR.

4.3. Remission and QoL

Patients who achieved FR, irrespective of SR, reported better QoL than did patients who did not achieve FR. Achieving SR without FR, however, was not associated with a better QoL. The association of FR with QoL suggests that FR is a desirable treatment goal for patients, family, and clinicians.

These results are in partial disagreement with those of Wunderink et al [8], who found that neither SR nor FR was

associated with QoL. This discrepancy may be caused by the levels of QoL in their sample of patients with first-episode psychosis, which were generally much higher than ours. Although Harvey and Bellack [6] suggest that “subjective well-being does not have a clear correlational relationship with other symptomatic and functional features of the illness,” our results indicate that FR is associated with better QoL, but that SR is not. By showing that SR tends to be of less importance for patients’ well-being than FR, our results thus contrast with those of other studies [14–17,33].

5. Limitations

Our results were based on 54% of all ACT patients with a psychotic disorder. Although we did not find statistical differences between both patient groups, except for sex, the generalizability of the results to all ACT patients treated in our center remains unknown. Also, our patient group differed from the patient groups in other studies, making it difficult to compare results, as stated above.

Another limitation of the work presented here is the missing data in our study. First, we had no data on PANSS assessments at baseline. Therefore, the true relation between patient and treatment characteristics and SR could not be properly assessed because we were not able to adjust for baseline values of SR. Second, the missing rate of self-reports on QoL was high (38.8%). We found no evidence of a relation between the missing self-reports and socio-demographic variables, although it is important to acknowledge that patients with missing self-reports tend to have more severe problems (FR). This means that the differences found in QoL scores between patients in FR and those not in FR may have been underestimated.

An important conceptual limitation of our study is that we used a specific definition of FR, based on 3 items of the HoNOS. Therefore, we acknowledge that our assessment of FR was a rather crude measure for FR. Although this definition is in line with the proposed criteria of FR [6,8], other studies used other scales for assessing FR. Using the HoNOS, however, has the advantage that this scale is widely used in clinical practice in many countries and easy to administer. In doing so, we feel that it is important to emphasize and underline the expert opinion of Mausbach and colleagues [34], who argue that we should try to use existing measures for assessing functioning that are already in routine use. New instruments with the sole purpose of measuring FR will increase the risk that these instruments will be used only in research but not in clinical practice. For this reason, we believe that HoNOS is an appropriate instrument to assess FR.

Apart from the question of which instrument to use for measuring FR (eg, the GAF, World Health Organization Disability Assessment Schedule, GSDS, HoNOS or another instrument), differences in cutoff levels are also important. We defined FR as the 3 relevant HoNOS items scoring 2 or lower (mild severity). However, FR might also be operationalized

more stringently, for example, using a cutoff score of 1 or lower (minimal severity). In that case, only 2.3% of our patients would have achieved FR (implying no or minimal disabilities). Using those criteria would mean that FR is nearly unachievable for patients receiving ACT, and therefore, these stringent criteria do not seem appropriate to assess FR.

Because we found higher FR rates than in other studies [29,30], this may suggest that our definition of FR was less stringent. In the absence of a consensus definition of FR, this remains unknown. We believe that our definition included important life domains (social functioning, daily life activities, and living conditions). It may be that when FR would be defined more stringently, for example, as having work, living independently, and having an appropriate social role, the proportion of patients achieving FR might be lower. After all, anyone in a job will plainly be hampered by severe psychotic symptoms. Thus, our outcomes concerning FR rates and its associations with SR are best understood as the result of the operationalization of FR, being proper housing, self-care, and social contacts. Following from this, it is clear that different assessment methods or cutoff criteria can result in discrepant findings (eg, 2.3% achieving FR and a different relation between FR and SR). However, we feel that it is very difficult and complex to create specific FR norms because no absolute reference exists and because these norms may be related to factors such as age or a downward economic situation.

6. Conclusions

Symptomatic remission was achieved by 26% of ACT patients after a mean period of 2½ years, and 30% reached FR. Symptomatic remission did not seem to be a prerequisite for FR or vice versa. Patients who achieved FR, irrespective of SR, reported better QoL than those who did not, supporting the choice of FR as a desirable treatment goal for patients, family, and clinicians.

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